2.02.16	Ultrasonographic Measurement of Carotid Intimal-Medial Thickness as an Assessment of Subclinical Atherosclerosis		
Original Policy Date:	December 7, 2006	**Effective Date:**	July 1, 2023
Section:	2.0 Medicine	**Page:**	Page 1 of 15

Policy Statement

I. Ultrasonographic measurement of carotid intima-media thickness (CIMT) as a technique for identifying subclinical atherosclerosis is considered **investigational** for use in the screening, diagnosis, or management of atherosclerotic disease.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Coding

The following CPT category I code specific to the combination of carotid intima-medial thickness (CIMT) and carotid atheroma evaluation:

- **93895**: Quantitative carotid intima media thickness and carotid atheroma evaluation, bilateral

Description

Ultrasonographic measurement of carotid intima-media (or intimal-medial) thickness (CIMT) refers to the use of B-mode ultrasound to determine the thickness of the 2 innermost layers of the carotid artery wall, the intima and the media. Detection and monitoring of intima-media thickening, which is a surrogate marker for atherosclerosis, may provide an opportunity to intervene earlier in atherogenic disease and/or monitor disease progression.

Related Policies

- Computed Tomography to Detect Coronary Artery Calcification
- Novel Biomarkers in Risk Assessment and Management of Cardiovascular Disease

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

In 2003, SonoCalc® (SonoSite) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. The FDA determined that this software was substantially equivalent to existing image display products for use in the automatic measurement of the IMT of the carotid

artery from images obtained from ultrasound systems. Subsequently, other devices have been cleared for marketing by the FDA through the 510(k) process.

FDA product code: LLZ.

Rationale

Background

Coronary Heart Disease

Heart disease is the leading cause of mortality in the United States, accounting for more than half of all deaths. Coronary heart disease (CHD), also known as coronary artery disease, is the most common cause of heart disease.[1] In a 2020 update on heart disease and stroke statistics from the American Heart Association, it was estimated that 605,000 Americans have a new coronary attack (first hospitalized myocardial infarction or CHD death) and 200,000 have a recurrent attack annually.

Established major risk factors for CHD have been identified by the National Cholesterol Education Program Expert Panel. These risk factors include elevated serum levels of low-density lipoprotein cholesterol and total cholesterol, and reduced levels of high-density lipoprotein cholesterol. Other risk factors include a history of cigarette smoking, hypertension, family history of premature CHD, and age.

Diagnosis

The third report of the National Cholesterol Education Program Adult Treatment Panel established various treatment strategies to modify the risk of CHD, with emphasis on target goals of low-density lipoprotein cholesterol. Pathology studies have demonstrated that levels of traditional risk factors are associated with the extent and severity of atherosclerosis. The third report of the National Cholesterol Education Program Adult Treatment Panel recommended use of the Framingham criteria to further stratify those patients with 2 or more risk factors for more intensive lipid management.[2] However, at every level of risk factor exposure, there is substantial variation in the amount of atherosclerosis, presumably related to genetic susceptibility and the influence of other risk factors. Thus, there has been interest in identifying a technique that can improve the ability to diagnose those at risk of developing CHD, as well as to measure disease progression, particularly for those at intermediate risk.

The carotid arteries can be well-visualized by ultrasonography, and ultrasonographic measurement of the carotid intima-media thickness (CIMT) has been investigated as a technique to identify and monitor subclinical atherosclerosis. B-mode ultrasound is most commonly used to measure the CIMT. CIMT is measured and averaged over several sites in each carotid artery. Imaging the far wall of each common carotid artery yields more accurate and reproducible CIMT measurements than imaging near wall. Two echogenic lines are produced, representing the lumen-intima interface and the media-adventitia interface. The distance between these 2 lines constitutes the CIMT.

Literature Review

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

Ultrasonographic Measurement of Carotid Intima-Media Thickness

Clinical Context and Test Purpose

The purpose of ultrasonographic measurement of carotid intima-media thickness (CIMT) is to provide a diagnostic option that is an alternative to or an improvement on existing tests, such as standard of care and alternative cardiovascular (CV) risk predictors, in patients who are undergoing cardiac risk assessment.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals who are undergoing cardiac risk assessment. This population may have other risk factors for coronary heart disease (CHD), including a history of cigarette smoking, hypertension, family history of premature CHD, and age.

Interventions

The test being considered is ultrasonographic measurement of CIMT. Ultrasonographic measurement of CIMT refers to the use of B-mode ultrasound to determine the thickness of the 2 innermost layers of the carotid artery wall, the intima and the media. Detection and monitoring of intima-media thickening, which is a surrogate marker for atherosclerosis, may provide an opportunity to intervene earlier in atherogenic disease and/or monitor disease progression.

Comparators

Comparators of interest include the standard of care and alternative CV risk predictors. Standard of care includes hypertension/blood pressure control and regular screenings. Alternative CV risk predictors commonly refer to the Framingham Risk Score, a gender-specific algorithm used to estimate the 10-year CV risk of an individual. The Framingham Risk Score was first developed based on data obtained from the Framingham Heart Study, to estimate the 10-year risk of developing CHD. In order to assess the 10-year cardiovascular disease (CVD) risk, cerebrovascular events, peripheral artery disease, and heart failure were subsequently added as disease outcomes for the 2008 Framingham Risk Score, on top of CHD.

Outcomes

The general outcomes of interest are test accuracy and morbid events. Possible negative outcomes include stroke, myocardial infarction (MI), and heart failure.

Table 1. Outcomes of Interest for Individuals Who Are Undergoing Cardiac Risk Assessment

Outcomes	Details	Timing
Test accuracy	Evaluating the efficacy of CIMT in assisting in the estimation of the risk of CVD using tools such as the Framingham Risk Score or the European systematic coronary risk evaluation	1 to 10 years
Morbid events	Cardiovascular events (e.g., MI, stroke, angina, vascular death)	5 to 10 years

CIMT: carotid intima-media thickness; CVD: cardiovascular disease; MI: myocardial infarction.

Study Selection Criteria

Below are selection criteria for studies to assess whether a test is clinically valid.

- The study population represents the population of interest. Eligibility and selection are described;
- The test is compared with a credible reference standard;
- If the test is intended to replace or be an adjunct to an existing test; it should also be compared with that test;
- Studies should report sensitivity, specificity, and predictive values. Studies that completely report true- and false-positive results are ideal. Studies reporting other measures (e.g., receiver operating characteristic, area under receiver operating characteristic, c-statistic, likelihood ratios) may be included but are less informative;
- Studies should also report reclassification of diagnostic or risk category.

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Review of Evidence

Systematic Reviews

Mookadam et al (2010) conducted a systematic review of the role of CIMT in predicting individual CV event risk and as a tool for assessing therapeutic interventions.[3,] Reviewers concluded that CIMT is an independent risk factor for CV events and may be useful in determining treatment when there is uncertainty regarding the approach or patient reluctance. However, they recommended further study to identify the best approaches to screening and interventions to prevent the progression of atherosclerosis.

In a meta-analysis, the USE Intima-Media Thickness collaboration investigators sought to determine whether common CIMT measurements can assist in estimating the 10-year risk of first-time MI or first-time stroke when added to the Framingham Risk Score.[4,] Den Ruijter et al (2012), using individual data for 45,828 patients from 14 population-based cohort studies, found that the risk of first-time MI or stroke was related positively to both the Framingham Risk Score and the adjusted common CIMT. The mean common CIMT was 0.73 mm, and it increased in every cohort with patient age during a median follow-up of 11 years. For every 0.1 mm difference in common CIMT, the hazard ratio (HR) for risk of MI or stroke, which occurred in 4007 patients, was 1.12 (95% confidence interval [CI], 1.09 to 1.14) for women and 1.08 (95% CI, 1.05 to 1.11) for men. However, adding common CIMT measurements to the Framingham Risk Score did not improve risk prediction and resulted in the reclassification of risk in only 6.6% of patients. The added value of mean common CIMT in reclassifying risk was only 0.8% (95% CI, 0.1% to 1.6%) and did not differ between men and women. The C statistic of the Framingham Risk Score model with and without CIMT was similar for men (0.759; 95% CI, 0.752 to 0.766) and women (0.757; 95% CI, 0.749 to 0.764), suggesting the addition of CIMT in risk assessment offered limited benefit.

Lorenz et al (2012), in another meta-analysis, pooled individual participant data from 16 studies (N=36,984) and examined CIMT progression from 2 ultrasound screenings taken 2 to 7 years apart (median, 4 years).[5,] Patients were followed for a mean of 7 years, during which time 1339 strokes, 1519 MIs, and 2028 combined endpoints (MI, stroke, vascular death) occurred. The mean CIMT of the 2 ultrasound results was predictive of CV risk using the combined endpoint (adjusted HR, 1.16; 95% CI, 1.10 to 1.22). In sensitivity analyses, no associations were found between CV risk and individual CIMT progression regardless of CIMT definition, endpoint, and adjustments. As an example, for the combined endpoints, an increase of 1 standard deviation in mean common CIMT progression resulted in an overall estimated HR of 0.97 (95% CI, 0.94 to 1.00) when adjusted for age, sex, and mean common CIMT; the HR was 0.98 (95% CI, 0.95 to 1.01) when adjusted for vascular risk factors. These data confirmed that CIMT is a predictor of CV risk but did not demonstrate that changes in CIMT over time are predictive of future events.

Van den Oord et al (2013) published a meta-analysis of 15 articles and found similar results on the added value of CIMT.[6,] Six cohort studies (N=32,299) were evaluated to examine the predictive value of CIMT when added to traditional CV risk factors. Although a CIMT increase of 0.1 mm was predictive for MI (HR, 1.15; 95% CI, 1.12 to 1.18) and stroke (HR, 1.17; 95% CI, 1.15 to 1.21), the addition of CIMT did not statistically improve risk prediction over traditional CV risk factors (p=.8).

Bytyc ̧i et al (2021) published a meta-analysis of 89 studies and found that CIMT was significantly higher in patients with CAD versus controls (p<.001).[7,] A moderate correlation was found between CIMT and severity of CAD (r = 0.60; 95% CI, 0.47 to 0.70; p<.001) and the number of diseased vessels (r = 0.49; 95% CI, 0.36 to 0.59; p<.001). A CIMT ≥ 1.0 mm had a summary sensitivity of 77% (range, 70% to 85%), summary specificity of 72% (range, 59% to 82%), positive predictive value of 82% (range, 80% to 83%), negative predictive value of 66% (range, 64% to 68%), and an accuracy of 76% (range, 74% to 77%) for predicting significant CAD.

Tschiderer et al (2020) published a meta-analysis of 7 prospective studies examining the extent to which CIMT predicts the incidence of carotid plaque in individuals free of carotid plaque at baseline.[8,] Results showed that when individuals in the top fourth of baseline CIMT distribution were compared with those in the bottom fourth, the relative risk for incidence of first-ever carotid plaque was 1.78 (95% CI, 1.53 to 2.07; p<.001).

Studies have found that including carotid plaques in CIMT measurements improved the predictive value of CV risk over CIMT assessed only in plaque-free sites.[9,10,11,12,] However, Lorenz et al (2012) found no difference in the main results between studies that included CIMT with carotid plaque and plaque-free CIMT.[5,] Peters et al (2012) found in their systematic review that adding carotid plaque to the traditional CIMT model increased the C statistic from 0.01 to 0.06.[13,]

Table 2. Systematic Reviews & Meta-Analysis Characteristics

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Lorenz et al (2012)[5,]	NR	16	Patients who were assessed with CIMT at least twice and followed up for MI, stroke, or death	36,984 (297 to 12,221)	Prospective, longitudinal, observational	NR
van den Oord et al (2013)[6,]	1997-2011	15	Patients at risk for CV events	76,201 (1734 to 14,214)	Observational studies	NR
Tschiderer et al (2020)[8,]	Through October 2019	7	Patients free of carotid plaque at baseline	9341	Prospective studies	mean, 8.7 y (range, 2 to 12 y)
Bytyc ̧i et al (2021)[7,]	Through September 2020	89	Patients with suspected or confirmed CAD	22,683	4 clinical trials; 85 observational studies	NR

CAD: coronary artery disease; CIMT: carotid intima-media thickness; CV: cardiovascular; MI: myocardial infarction; NR: not reported.

Table 3. Systematic Reviews & Meta-Analysis Results

Study	CIMT Progression HR (95% CI)	Association of CIMT with CV risk HR (95% CI)
Lorenz et al (2012)[5,]	0.97[a] (0.94 to 1.00)	1.16 (1.10 to 1.22)
		Association of 1 SD (0.1 mm) increase in CIMT with future MI HR (95% CI)
van den Oord et al (2013)[6,]	NR	1.26 (1.20 to -1.31)
		Association of top vs. bottom fourth of baseline CIMT with first-ever carotid plaque RR (95% CI)

Study	CIMT Progression HR (95% CI)	Association of CIMT with CV risk HR (95% CI)
Tschiderer et al (2020)[8,]	NR	1.78 (1.53 to 2.07)
		Association of CIMT with CAD WMD (95% CI)
Bytyc¸i et al (2021)[7,]	NR	-0.18 (-0.16 to -0.21)

CAD: coronary artery disease; CI: confidence interval; CIMT: carotid intima-media thickness; CV: cardiovascular; HR: hazard ratio; MI: myocardial infarction; NR: not reported; RR: relative risk; SD: standard deviation; WMD: weighted mean difference.
[a] When adjusted for age, sex, and mean common CIMT.

Prospective Cohort Studies

Numerous prospective cohort studies have evaluated the association between CIMT and future CV events. Some of the larger trials are discussed below. For example, in the Atherosclerosis Risk in Communities study, trialists evaluated risk factors associated with increased CIMT in 15,800 subjects.[14,]The CIMT had a graded relation with increasing quartiles of plasma total cholesterol, low-density lipoprotein cholesterol, and triglycerides. The CIMT also correlated with the incidence of CHD in a subgroup of patients enrolled in the trial after 4 to 7 years of follow-up.[15,] Among the 12,841 individuals studied, there were 290 incident events. The HR rates for women and men, adjusted for age and sex, comparing extreme CIMT (ie, ≥ 1 mm) with nonextreme CIMT (ie, < 1 mm), were 5.07 for women and 1.85 for men. The strength of the relation was reduced by including major CHD risk factors but remained elevated for higher measurements of CIMT. The authors concluded that mean CIMT was a noninvasive predictor of future CHD incidence.

The Rotterdam cohort study started in 1989 and recruited 7983 men and women ages 55 years and older.[16,] Its main objective was to investigate the prevalence and incidence of risk factors for chronic diseases, including CVD, in older adults. One aspect of the study sought to determine whether the progression of atherosclerosis in asymptomatic elderly subjects is a prelude to CV events. Measurements of CIMT were used to assess the progression of atherosclerosis. Increasing CIMT was associated with increased risks of stroke and MI.

O'Leary et al (1999) performed CIMT measurement on 4476 asymptomatic subjects aged 65 years or older without clinical CVD in the Cardiovascular Health Study.[17,] The incidence of CV events correlated with measurements of CIMT; this association remained significant after adjusting for traditional risk factors. The authors concluded that increases in CIMT were directly associated with an increased risk of MI and stroke in older adults without a history of CVD.

The longitudinal Carotid Atherosclerosis Progression Study included 4904 subjects. All subjects received a baseline CIMT measurement as well as a traditional risk factor analysis and were followed for 10 years (mean follow-up, 8.5 years; range, 7.1 to 10 years). Adverse events were MI in 73 (1.5%) patients, angina or MI in 271 (5.5%) patients, and death in 72 (1.5%) patients. Lorenz et al (2010) retrospectively reviewed Carotid Atherosclerosis Progression Study data.[18,] They modeled the predictive value of CIMT on adverse events within that decade. Because the thresholds of CIMT measurements that would lead to a reclassification of risk are unknown, the authors used 24 models of reclassification and 5 statistical tests. Each model compared the predictive value of traditional risk factors alone with those risk factors plus CIMT. None of the reclassification models improved with the addition of CIMT measurements. Investigators concluded that their retrospective analysis did not support the use of CIMT as a clinically useful risk classification tool when used with traditional risk factor analysis.

In the Multi-Ethnic Study of Atherosclerosis (MESA) trial, an ongoing cohort study of atherosclerosis, CIMT was found to be a modestly better predictor of stroke, but it was a worse predictor of CHD than coronary artery calcium (CAC) score at a median follow-up of 3.9 years among 6698 adults asymptomatic at baseline.[19,] Paramsothy et al (2010), also reporting on the MESA trial,

compared CIMT results in 4792 healthy individuals (nondiabetic adults not on lipid-lowering medications) across 6 different lipid groups, including normolipemia and several types of common dyslipidemias.[20,] Mean CIMT values were increased only for the combined hyperlipidemia (defined as any high-density lipoprotein cholesterol level, low-density lipoprotein cholesterol ≥ 160 mg/dL, and triglycerides ≥ 150 mg/dL) and simple hypercholesterolemia (defined as any high-density lipoprotein cholesterol level, low-density lipoprotein cholesterol ≥ 160 mg/dL, and triglycerides < 150 mg/dL) groups. Blaha et al (2011) published another MESA report assessing 6760 patients with elevated high-sensitivity C-reactive protein as defined by the Justification for the Use of Statins in Primary Prevention: An Intervention Trial Evaluating Rosuvastatin study; they found CIMT increases correlated with obesity but only mildly with high-sensitivity C-reactive protein.[21,] Patel et al (2015) also reported on the MESA trial, which evaluated 6125 individuals with a family history of premature CHD, and identified 382 atherosclerotic CVD events at a mean follow-up of 10.2 years.[22,] The study found that CAC data improved the risk estimation of atherosclerotic CVD events, but CIMT did not.

Camhi et al (2011) reported on the Bogalusa Heart Study (N = 991) and found that obesity along with overweight and elevated metabolic risk were associated with increased CIMT.[23,] They also reported that in this study population, 41% of patients had increased CHD risk. In a study evaluating the association between clotting factor VII and CIMT (Coronary Artery Risk Development in Young Adults [CARDIA] study), clotting factor VII was associated with increases in CIMT in 1254 subjects.[24,]

Baber et al (2015) reported on the BioImage study, which enrolled 5808 asymptomatic individuals from the U.S. [25,] All patients were evaluated by 3-dimensional carotid ultrasound and by CAC score and followed for a median of 2.7 years. The primary endpoint was major CV events, defined as CV death, MI, and ischemic stroke. Carotid plaque burden was an independent predictor of outcomes, with an HR of 2.36 (95% CI, 1.13 to 4.92) for individuals in the highest tertile. The CAC score was also an independent predictor of outcomes, with HRs similar to carotid plaque. Both carotid plaque and CAC score led to significant net reclassification, with a net reclassification index of 0.23.

Geisel et al (2017) conducted a prospective cohort study of 3108 patients without CVD upon entrance to the study.[26,] All patients were evaluated for traditional risk factors of CVD; they were also assessed to calculate the CIMT, CAC score, and Ankle-Brachial Index score. During a mean follow-up of 10 years, 223 individuals suffered a major CV event (coronary event, stroke, CV death). All 3 methods helped predict adverse CV events. While CIMT was found to be higher in those who experienced an adverse CV event (0.76) than those who did not (0.69), CIMT did not significantly improve the prediction of cardiac risk for patients with an intermediate Framingham Risk Score.

Villines et al (2017) prospectively assessed a cohort of 3801 African American patients free of CVD at baseline.[27,] Over a median follow-up of 9 years, there were 171 new cases of CVD and 339 deaths. The incidence of CV events correlated with changes in CIMT and participants in the highest CIMT quartile had the largest unadjusted incident rates of CVD for both men and women. However, risk reclassification improved only slightly when adding CIMT to a model that included only traditional risk factors for CVD.

Table 4. Summary of Key Prospective Cohort Clinical Validity Study Characteristics

Study	Study Population	Study Type	Country	Dates	Follow-Up
Chambless et al (1997)[15,]	Asymptomatic for CHD	Prospective	US	1987-1993	Median 5.2 y
O'Leary et al (1999)[17,]	Asymptomatic for CHD; ≥ 65 y	Prospective	US	1989-1993	Median 6.2 y
van der Meer et al (2004)[16,]	Asymptomatic for CHD; ≥ 55 y	Cohort	EU	1990-1993	NR

Study	Study Population	Study Type	Country	Dates	Follow-Up
Folsom et al (2008)[19,]	Initially free of CVD	Cohort	US	2000-2007	Median 3.9 y
Baber et al (2015)[25,]	Asymptomatic for CVD	Cohort	US, EU	2008-2009	Median 2.7 y
Lorenz et al (2010)[18,]	Initially free of CVD	Retrospective	EU	NR	10 y
Geisel et al (2017)[26,]	Initially free of CVD	Prospective	EU	2000-2003	Mean 10.3 ± 2.8 y
Villines et al (2017)[27,]	African Americans without CVD	Prospective	US	2000-2011	Median 9 y

CHD: coronary heart disease; CVD: cardiovascular disease; EU: Europe; NR: not reported; US: United States.

Section Summary: Clinically Valid

Evidence from large, prospective cohort studies and systematic reviews has established that CIMT is an independent risk factor for CAD. However, systematic reviews have shown that the use of CIMT data to reclassify patients into clinically relevant categories is modest and may not be clinically important. The uncertainty concerning the ability to reclassify patients into clinically relevant categories limits the potential for CIMT to improve health outcomes.

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, more effective therapy, or avoid unnecessary therapy or testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials (RCTs).

Johnson et al (2011) conducted a study in which 55 patients, aged ≥ 40 years with 1 or more CAD risk factors, received carotid ultrasound screenings to determine prospectively whether abnormal results would change physician and patient behaviors.[28,] Results were considered abnormal (when CIMT was > 75th percentile or with the presence of carotid plaque) in 266 patients. Self-reported questionnaires were completed before the carotid ultrasound, immediately after the ultrasound, and 30 days later to assess behavioral changes. Physician behavior in prescribing aspirin (p<.001) and cholesterol medication (p<.001) changed significantly after the identification of abnormal carotid ultrasound results. Abnormal ultrasound results predicted reduced dietary sodium (odds ratio [OR], 1.45; p=.002) and increased fiber intake (OR, 1.55; p=.022) in patients, but no other significant changes. Health outcomes were not evaluated in this study, and the short-term follow-up limits the interpretation of results.

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.
The evidence on the reclassification of CV risk offers a potential chain of evidence to improve outcomes. If a measure helps reclassify patients into risk categories that have different treatment approaches, then clinical management changes may occur that lead to improved outcomes. Because the ability to reclassify patients into clinically relevant categories with CIMT is modest at best, the clinical utility of this measure for reclassification is uncertain.

One study, however, aimed to estimate "normal" CIMT progression in order to identify subjects with faster atherosclerosis development. Olmastroni et al (2019) analyzed 1175 participants (36% men; mean age, 53 ± 11 years at baseline) with low to moderate CV risk.[29,] The participants underwent 4 clinical evaluations and ultrasound CIMT determinations approximately every 4 years. Investigators

assessed the growth of CIMT for each participant across the 12 years of the study using growth curve modeling. Results showed age to be the major factor in the significant slope observed for both mean CIMT and maximum CIMT models (mean: β = 0.01, p<.001; maximum: β = 0.013, p<.001). Sex also affected mean and maximum CIMT, with higher levels in men (mean: β = −0.027, p<.001; maximum: β = −0.033, p<.001). In addition, the age-dependent growth patterns differed between men and women. For women, menopausal status affected slopes. Women who were in menopause at the start of the study or who went through menopause during the follow-up had mean and maximum CIMT slopes that were similar to men's. Women with fertile status over the course of the study period progressed slowest. Other factors, such as smoking, systolic blood pressure, fasting glucose, and the presence of carotid atherosclerosis, predicted the speed of progression of both mean and maximum CIMT. The investigators noted that different mean and maximum CIMT curve slopes were seen in participants developing both carotid wall thickening and focal carotid atherosclerosis compared with the other participants. The results of this study demonstrated that estimated standard CIMT curves could be a useful tool for determining CV risk in asymptomatic low to intermediate-risk patients, allowing for earlier and more individualized preventive measures.

Section Summary: Clinically Useful

There is no direct evidence of the clinical utility of measuring CIMT for cardiac risk stratification. The available evidence on reclassification into clinically relevant categories does not indicate that the use of CIMT will improve health outcomes. The objective of 1 study, however, was to define standard CIMT progression in low to moderate CV risk patients. Study results showed definite patterns related to various factors that could be used as a tool to earlier identify patients at increased CV risk.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Cardiology and American Heart Association

In 2013, the guidelines from the American College of Cardiology and the American Heart Association on the assessment of cardiovascular (CV) risk did not recommend carotid intima-media thickness (CIMT) measurement in routine risk assessment of a first atherosclerotic CVD event (class III: no benefit; level of evidence: B).[30,] This differs from their 2010 joint guidelines for the assessment of CV risk, which indicated that CIMT might be reasonable for assessing CV risk in intermediate-risk asymptomatic adults.[31,]

American Association of Clinical Endocrinologists

In 2017, the American Association of Clinical Endocrinologists and American College of Endocrinology published guidelines stating that CIMT could be applied as a risk stratification tool in determining the need for more aggressive preventive strategies against CVD (grade B; best evidence level 2), but not routinely.[32,]

American Society of Echocardiography

In 2008, the American Society of Echocardiography (ASE) consensus statement,[33,] endorsed by the Society for Vascular Medicine, stated that CIMT is a feature of arterial wall aging "that is not synonymous with atherosclerosis, particularly in the absence of plaque." The statement recommended measurement of both CIMT and carotid plaque by ultrasound "for refining CVD risk assessment in patients at intermediate CVD risk (Framingham Risk Score 6% to 20%) without

established CHD [coronary heart disease], peripheral arterial disease, cerebrovascular disease, diabetes mellitus, or abdominal aortic aneurysm." However, the Society acknowledged that "More research is needed to determine whether improved risk prediction observed with CIMT or carotid plaque imaging translates into improved patient outcomes." The recommendations made in the 2008 consensus statement were endorsed in ASE's 2020 guideline entitled *Recommendations for the Assessment of Carotid Arterial Plaque by Ultrasound for the Characterization of Atherosclerosis and Evaluation of Cardiovascular Risk.*[34,] Authors of the 2020 guideline also note the following: "Since the largest portion of CIMT (approximately 99% in healthy individuals and approximately 80% when diseased) consists of the medial layer, CIMT has not been shown to consistently add to CVD risk prediction."

U.S. Preventive Services Task Force Recommendations

In 2009, the U.S. Preventive Services Task Force (USPSTF) published a systematic review of CIMT within the scope of a larger recommendation on the use of nontraditional risk factors in CHD risk assessment.[35,] The USPSTF could not draw conclusions on the applicability of CIMT to the intermediate-risk population at large outside the research setting. The USPSTF summary of recommendations specific to CIMT stated that: "... the current evidence is insufficient to assess the balance of benefits and harms of using ... [CIMT] ... to screen asymptomatic men and women with no history of CHD to prevent CHD events." The USPSTF identified the following research need: "The predictive value ... of carotid IMT ... should be examined in conjunction with traditional Framingham risk factors for predicting CHD events and death."

In 2018, the USPSTF published a recommendation statement on using nontraditional risk factors to assess the risk of CVD; CIMT was not mentioned in this recommendation.[36,]

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in Table 5.

Table 5. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT03314818[a]	BioImage 2: Long-Term Follow-up of BioImage Study Cohort to Investigate Natural History of Carotid Plaque as Determined by 3D Ultrasound	1000	Oct 2023
NCT02508454[a]	The Miami Heart Study at Baptist Health South Florida: A Prospective Study of Sub-Clinical Cardiovascular Disease and Emerging Cardiovascular Risk Factors in Asymptomatic Young and Middle-Aged Adults	4000	Sep 2024
NCT01849575	Direct VIsualiZAtion of Asymptomatic Atherosclerotic Disease for Optimum Cardiovascular Prevention. A Population Based Pragmatic Randomised Controlled Trial Within Västerbotten Intervention Programme (VIP) and Ordinary Care (VIPVIZA)	3532	Dec 2027

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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Documentation for Clinical Review

- No records required

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	93895	Quantitative carotid intima media thickness and carotid atheroma evaluation, bilateral

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
12/07/2006	New Policy Adoption
04/02/2010	Policy revision without position change Coding update
08/06/2013	Policy revision without position change. Policy placed on No Further Routine Literature Review and Update status.
09/30/2014	Policy title change from Carotid Intima-Media Thickness Measurement Policy revision without position change
01/01/2015	Coding update
01/01/2017	Policy revision without position change
03/01/2017	Policy revision without position change
07/01/2018	Policy revision without position change
07/01/2019	Policy revision without position change
07/01/2020	Annual review. No change to policy statement. Literature review updated.
01/01/2021	Coding update
07/01/2021	Annual review. No change to policy statement. Policy guidelines and literature updated.
07/01/2022	Annual review. No change to policy statement. Policy guidelines and literature updated.

Effective Date	Action
07/01/2023	Annual review. No change to policy statement. Literature review updated.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT (No changes)	
BEFORE	**AFTER**
Ultrasonographic Measurement of Carotid Intimal-Medial Thickness as an Assessment of Subclinical Atherosclerosis 2.02.16 **Policy Statement:** I. Ultrasonographic measurement of carotid intima-media thickness (CIMT) as a technique for identifying subclinical atherosclerosis is considered **investigational** for use in the screening, diagnosis, or management of atherosclerotic disease.	**Ultrasonographic Measurement of Carotid Intimal-Medial Thickness as an Assessment of Subclinical Atherosclerosis 2.02.16** **Policy Statement:** I. Ultrasonographic measurement of carotid intima-media thickness (CIMT) as a technique for identifying subclinical atherosclerosis is considered **investigational** for use in the screening, diagnosis, or management of atherosclerotic disease.